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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

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09/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	09/965,697	DHADIALLA ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 August 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 35 USC 112, lack of enablement, claim 11.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-4,7-10,12 and 15*.
   Claim(s) withdrawn from consideration: *21-46*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See below.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Manjunath N. Rao /
Supervisory Patent Examiner, Art Unit 1647

/Shulamith Shafer/
Patent Examiner, AU 1647

Applicants' amendment of 8/24/09 are acknowledged and made of record. Claims 1, 2, 7, 9 and 10 have been amended and the amendment made of record. Claims 11, 48 and 49 are canceled.

Claims 1-4, 7-10, 12, 15, 21-46 are pendiing in the instant application. Claims 21-46 remain withdrawn as being drawn to a non-elected invention.

The rejection of Claim 11 under 35 USC 112, 1st paragraph, lack of enablement is withdrawn in light of applicants' cancellation of the claim.

The amendment to Claim 1, and 9 is sufficient to overcome the rejection of the claims 1-4, 7-10, 12 and 15 under 35 USC 112, 1st paragraph, written description, in part. The claims have been amended to recite a multiple inducible gene regulation system consisting of two orthogonal gene regulation systems; thus, the part of the rejection directed recitation of more than two gene regulation systems is withdrawn.

However, the claims are still rejected under 35 USC 112, 1st paragraph, as failing to comply with written description requirement for reasons of record and reasons set forth below.

The claims are directed to a genus of an essentially unlimited scope of multiple gene regulation systems comprising two individually operable gene regulation systems, wherein each individual system operates independently of any other ("is orthogonal"). However, the only systems described are ones comprising a Lepidopteran/Dipteran and a Lepidopteran/Homopteran ecdysone receptor system. Applicant has not identified any particular structure of the ligand binding domains of the components of the gene regulation system that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, but has identified the claimed systems solely by a function.

The claims encompass systems comprising the ligand binding domains (LBD) of any Group H nuclear receptor and the LBD of any nuclear receptor capable of forming a dimer with said Group H nuclear receptor LBD.

The specification teaches the genus of Group H nuclear receptors consist of numerous species including: ecdysone receptor, ubiquitous receptor (UR), Orphan receptor 1 (OR-1), steroid hormone nuclear receptor 1 (NER-1), RXR interacting protein-15 (RIP-15), liver x receptor .beta. (LXR.beta.), steroid hormone receptor like protein (RLD-1), liver x receptor (LXR), liver x receptor .alpha. (LXR.alpha.), farnesoid x receptor (FXR), receptor interacting protein 14 (RIP-14), and farnesol receptor (HRR-1) [paragraph 0148]. The second nuclear receptor ligand binding domain also comprises numerous species: a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain [paragraph 0158]. Thus, the amended claims are directed to a genus of multiple gene regulation systems comprising numerous species of two individually operable gene regulation systems, wherein each individually system operates independently of any other ("is orthogonal").

The skilled artisan would not recognize that applicants were in possession of a genus of multiple expression systems. Applicants have not identified any particular chemical structure that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, but have identified the claimed systems solely by a function.

Pages 40-43 of the specification [paragraphs 0204-0240], disclose complex, art-recognized methods of searching for specific ligands and screening for novel cognate LBDs. The structures of ligands presented on page 40, as potential chemotypes ideal for use as ligands, comprise a natural ecdysteroid and a known diacylhydrazine. These compounds appear to be cross-interactive across insect species, which is contrary to that required by the claimed invention, that the multiple systems be orthogonal. Applicants teach that "an orthogonal ligand/receptor set does not exist within these two structural families". This is certainly not evidence of possession but indicates that to achieve the goal of a multiple, orthogonal gene regulation system, as broadly claimed, further experimentation is required (page 40, lines 8-15, paragraph 0205).

Thus, applicants have not disclosed any additional molecules as ligands nor have they identified any particular cognate LBDs. The methods outlined act as an invitation to design and discover which ligands-receptor pairs may work as the multiple gene regulatory systems of the instant invention.

Applicants' teachings are an invitation to experiment to design, identify and isolate appropriate receptor/ligand pairs which act orthogonally; the disclosure does not provide evidence that Applicants were in possession of such. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features.

An invitation for others to discover a representative number of species with known or disclosed correlation between function and structure of the polynucleotides or polypeptides of gene modulation systems or by a combination of such identifying characteristics does not reasonably provide one of skill in the art with sufficient information to reasonably visualize or predict which ligand/receptor pairs would be encompassed by the claims. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See University of Rochester, 38 F.3d at 927, 69 USPQd at 1895. Without a correlation between structure and function the claim does little more than define the claimed invention by function. That is not sufficient to define a genus because it is only an indication of what the gene or ligand does, rather than what it is, see, Eili Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

Applicants are not in possession of the claimed genus of "multiple inducible gene modulation system" and thus, the current claims do not comply with the requirement for written description under 35 USC 112, first paragraph.

Therefore, the Lepidopteran/Dipteran and Lepidopteran/Homopteran receptor schemes (of the Group H family of receptors) but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Applicants arguments traversing the rejection have been carefully considered but have not been found to be persuasive for reasons of record.